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# Synthesis of some esters of alpha-dialkylphosphono-beta-trichloroethyl phosphoric acid and derivatives of pyrophosphoric acid.

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The present paper is in two parts. The first part deals with synthesis of alpha-dialkylphosphono-beta-trichloroethyl didalkyl phosphates.

Recently the attention of Russian and foreign chemists has been directed to the study of the reaction between chloral and trialkyl phosphites.

This reaction was first realized in Kazan by A.E.Arbuzov and F.I.Alimova (1). Then it was studied by Perkow (2). He showed that the reaction does not yield normal products of the Arbuzov rearrangement which contain the P-C bond, but leads to formation of the dialkyl beta-dichlorovinyl phosphates:

$$(RO)_2P(O)OCH{:}CCl_2$$

Soon other papers appeared. These were devoted to the study of the reaction of chloral with dialkyl phosphites (3).

By means of this reaction there were prepared the corresponding alpha-hydroxy-beta-trichloroethyl dialkyl phosphonates:

$$(RO)_2P(O)CH(OH)CCl_3$$

These in turn can lose a mole of hydrogen chloride by the action of aqueous or alcoholic solutions of alkalies and be rearranged into dialkyl beta-dichlorovinyl phosphates (4).

In the present paper there was undertaken the attempt to realize the reaction between alpha-hydroxy-beta-trichloroethyl dialkyl phosphonates and various chlorides of dialkyl phosphoric acids.

The initial alpha-hydroxy-beta-trichloroethylphosphonates (diethyl and dimethyl) were prepared from chloral and dimethyl or diethyl phosphite respectively by the method of Barthel and coworkers (3) with the small difference that the crude hydroxyphosphonate was recrystallized not from a mixture of petroleum ether and small amount of benzene, but from cyclohexane.

Synthesis of the alpha-dialkylphosphono-beta-trichloroethyl dialkyl phosphates was realized according to the following equation:

$$(RO)_2P(O)CH(OH)CCl_3 + ClP(O)(OR')_2 + (C_2H_5)_3N \rightarrow (RO)_2P(O)CH(CCl_3)OP(O)(\ldots)$$

R= Me, Et; R'=Et, Pr, iso-Pr, Bu, iso-Bu $\qquad (C_2H_5)_3\overset{+}{N}.HCl$

This reaction could be run successfully in the medium of ethyl ether, benzene, gasoline or cyclohexane by stirring the reaction mixture made up of equimolar amounts of the materials for several hours.

The reaction proceeds rather sluggishly at room temperature. Heating to 35-50° permits its acceleration and the contraction of the reaction period from 12-15 to 4-5 hours. The isolation of the final product of the reaction and its purification were performed as usual: triethyl amine hydrochloride was filtered off, the solvent was removed and then a vacuum distillation was run. In some cases the preliminary purification of the crude reaction product was realized either by molecular distillation or by two or three washings with water with subsequent drying over sodium sulfate (table 1).

the newly prepared esters were rather mobile colorless liquids with a weak, unpleasant odor.

The initial tests of these preparations in their action of grain weevil were carried out in the entomological laboratory of Kazan Section of the Academy of Sciences USSR by M.A.Kudrina; these showed that all these esters were considerably more powerful insecticidal substances than DDT. In their contact action they approach such organophosphorus insecticides as tetraethyl pyrophosphate, its mono-thiono analog and parathion.

It is rather interesting that compounds of this type turned out to be insecticides with intraplant or systemic action against chewing insects. This property was discovered by the senior scientific coworker of the Institute of Fertilizers and Insectofungicides named after A.V.Samoilov, E.A.Pokrovskii, whose studied the action of diethylphosphono trichloroethyl diisopropyl phosphate on the chewing insects and suggested the study of these compounds on a broader base.

The work on synthesis of this type and the study of their physiologic properties will be continued.

The second part of the paper deals with work in the area of synthesis of some derivatives of pyrophosphoric acid. The study of properties of esters of pyrophosphoric acid, their sulfur and their nitrogen containing analogs showed that the majority of these compounds have strong physiological action including the insecticidal action.

Some representatives of this class of compounds, for example, tetraethyl pyrophosphate, octamethyl pyrophosphoramide, finds application in agriculture (5). Others, for example, tetraethyl monothiopyrophosphate are simultaneously powerful insecticidal and interesting medicinal preparations (agents for treatment of glaucoma and other diseases).(6,7).

Synthesis of various derivatives of pyrophosphoric acid can yield new interesting( from physiological side) preparations.

Table 1.

Formulas of compounds prepared, their basic physical constants and analytical results.

| No. | Formula | Boiling pt. | $n_D^{20}$ | $d_4^{20}$ | Yield, % | $MR_D$ Cal. | $MR_D$ Found | P analys. % Calc. | P analys. % Fou. |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $(EtO)_2P(O)CH(CCl_3)OP(O)(OEt)_2$ | 126-8/0.03 | 1.4642 | 1.3551 | 63.1 | 85.76 | 85.86 | 14.7 | 14. 14. |
| 2 | $(EtO)_2P(O)CH(CCl_3)OP(O)(OPr)_2$ | 139-40/0.02 | 1.4580 | 1.290 | 58.2 | 94.98 | 95.03 | 13.8 | 13. |
| 3 | $(EtO)_2P(O)CH(CCl_3)OP(O)(OPr\text{-}iso)_2$ | 129-31/0.02 | 1.4606 | 1.304 | 57.0 | 94.98 | 94.54 | 13.8 | 13. |
| 4 | $(EtO)_2P(O)CH(CCl_3)OP(O)(OBu)_2$ | 145-8/0.03 | 1.4422 | 1.214 | 66.6 | 104.3 | 104.2 | 13.0 | 13. |
| 5 | $(EtO)_2P(O)CH(CCl_3)OP(O)(OBu\text{-}iso)_2$ | 140-2/0.05 | 1.4635 | 1.2657 | 53.5 | 104.3 | 104.0 | 13.0 | 13. |
| 6 | $(EtO)_2P(O)CH(CCl_3)OP(O)(NMe_2)_2$ | 139-42/0.05 | 1.4682 | 1.1219 | 34.8 | 90.15 | 90.1 | 14.75 | 14. 13. |
| 7 | $(EtO)_2P(O)CH(CCl_3)OP(S)(OEt)_2$ | 136-9/0.03 | 1.4572 | 1.3036 | 41.1 | 91.04 | 90.9 | 14.2 | 14. 14. |
| 8 | $(MeO)_2P(O)CH(CCl_3)OP(O)(OEt)_2$ | 119-21/0.05 | 1.4590 | 1.4128 | 55.5 | 76.81 | 76.1 | 15.8 | 15. 16. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 9 | $(MeO)_2P(O)CH(CCl_3)OP(O)(OPr)_2$ 120-2/0.02 | 1.4506 | 1.3228 | 50.5 | 85.75 | 85.73 | 14.7 | 14.<br>14. |
| 10 | $(MeO)_2P(O)CH(CCl_3)OP(O)(OPr\text{-}iso)_2$ 116-7/0.05 | 1.4540 | 1.2880 | 41.5 | 85.75 | 85.62 | 14.7 | 14.<br>14. |
| 11 | $(MeO)_2P(O)CH(CCl_3)OP(O)(OBu)_2$ 132-3/0.02 | 1.4515 | 1.2698 | 32.0 | 95.18 | 96.08 | 13.8 | 14.<br>14.3 |
| 12 | $(MeO)_2P(O)CH(CCl_3)OP(O)(OBu\text{-}iso)_2$ 129-32/0.02 | 1.4608 | 1.3047 | 52.5 | 95.18 | 94.50 | 13.8 | 13.6<br>13. |

Our small study of this area - synthesis of ester amides of pyrophosphoric acid was realized by the reaction of chlorids of tetramethyldiamidophosphoric acid with various dialkyl thiophosphates. In this case there were formed dialkyl tetramethyldiamido thiopyrophosphates. Analogously, from the chlorids of tetraethyldiamidothiophosphoric acid were synthesized, with the appropriate dialkyl thiophosphates, the dialkyl tetraethyldiamido dithiopyrophosphates shown in table 2. All the newly prepared compounds were mobile, colorless liquids with weak unpleasant odor.

Table 2

Some constants of the prepared compounds.

| No. | Formula | Boiling pt. | $n_D^{20}$ | $d_4^{20}$ | Yield % | MR Calc. | MR Found | P analysis, % Calcd. | P analysis, % Found |
|---|---|---|---|---|---|---|---|---|---|
| 1 | $(Me_2N)_2P(O)OP(S)(OPr)_2$ | 150-60/4 | 1.4700 | 1.119 | 58 | 82.15 | 82.75 | 18.7 | 18.6<br>18.59 |
| 2 | $(Me_2N)_2P(O)OP(S)(OPr\text{-}iso)_2$ | 150-3/3 | 1.4665 | 1.124 | 48 | 82.15 | 81.8 | 18.7 | 19.4<br>19.1 |
| 3 | $(Me_2N)_2P(O)OP(S)(OBu)_2$ | 154-7/1 | 1.4695 | 1.097 | 45 | 91.38 | 91.39 | 17.2 | 17.3<br>17.3 |
| 4 | $(Me_2N)_2P(O)OP(S)(OBu\text{-}iso)_2$ | 159.5/2.5 | 1.4652 | 1.082 | 50 | 91.38 | 91.96 | 17.2 | 17.4<br>17.28 |
| 5 | $(Et_2N)_2P(S)OP(S)(OEt)_2$ | 183-6/2 | 1.500 | 1.210 | 44 | 99.75 | 99.65 | 16.5 | 16.5<br>16.7 |
| 6 | $(Et_2N)_2P(S)OP(S)(OPr)_2$ | 187-70/2 | 1.4970 | 1.099 | 49 | 108.6 | 108.6 | 15.3 | 15.1<br>15.1 |
| 7 | $(Et_2N)_2P(S)OP(S)(OPr\text{-}iso)_2$ | 165-8/2-3 | 1.4912 | 1.078 | 36 | 108.6 | 108.8 | 15.3 | 15.3<br>15.31 |
| 8 | $(Et_2N)_2P(S)OP(S)(OBu)_2$ | 170-5/2 | 1.4960 | 1.068 | 25 | 117.8 | 118.2 | 14.2 | 14.35 |
| 9 | $(Et_2N)_2P(S)OP(S)(OBu\text{-}iso)_2$ | 173-7/2 | 1.4880 | 1.060 | 30 | 117.8 | 117.5 | 14.3 | 14.05<br>14.40 |

Compounds of this type, as shown by preliminary tests done in the Kazan Section of the Academy of Sciences USSR and in the Scientific Institute for Fertilizers and Insectofungicides, named after Ya.V.Samoilov (Moscow), are insecticidal substances with contact and intraplant action. In their properties as intraplant insecticides they approach octamethylpyrophosphoramide.

Along with the prepartion of various esters amides of pyrophosphoric we also set up a goal of synthesis of some alkyl 2-chloroethyl derivatives of this acid.

Table 3

Formulas of the synthesized alkyl 2-chloroethyl esters of pyrophosphoric acid and some of their constants

| No. | Formula | Boiling pt. | $n_D^{20}$ | $d_4^{20}$ | Yield % | P analysis Calc. | P analysis Found | Insecticidal action on grain weevil Conc. % | Insecticidal action on grain weevil Day | Insecticidal action on grain weevil K |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $(ClCH_2CH_2O)(EtO)P(O)OP(O)(OEt)_2$ | 136-7/0.02 | 1.4350 | 1.2775 | 47 | 19.4 | 19.3 | 0.05 | 2 | 1 |
| | | | | | | | | 0.1 | 1 | 1 |
| 2 | $(ClCH_2CH_2O)_2P(O)OP(O)(OEt)_2$ | 164-5/0.02 | 1.4490 | 1.3578 | 45 | 17.2 | 17.2 | 0.05 | 5 | 9 |
| | | | | | | | | 0.01 | 3 | 1 |
| | | | | | | | | 0.5 | 1 | 1 |
| 3 | $(ClCH_2CH_2O)_2P(O)OP(O)(OEt)OCH_2CH_2Cl$ crude | | 1.4636 | 1.4209 | 94 | - | - | 0.1 | 2 | |
| | | | | | | | | 0.5 | 2 | |
| | | | | | | | | 1 | 2 | |
| 4 | $(ClCH_2CH_2O)_2P(O)OP(O)(OCH_2CH_2Cl)_2$ crude | | 1.4755 | 1.4454 | 81 | 14.4 | 14.3 | 0.5 | 7 | |
| | | | | | | | | 1 | 7 | 1 |
| 5 | $[(ClCH_2CH_2O)(EtO)P(O)]_2O$ | 145-5.5/0.02 | 1.4450 | 1.3240 | 20 | 17.2 | 16.9 | 0.1 | 7 | 2 |
| | | | | | | | | 0.5 | 7 | 6. |
| 6 | $[(ClCH_2CH_2O)(PrO)P(O)]_2O$ | 162.5-3/0.03 | 1.4490 | 1.2759 | 35 | 16.8 | 16.1 | 0.05 | 5 | 1 |
| | | | | | | | | 0.1 | 5 | 3 |
| | | | | | | | | 0.5 | 5 | 9 |
| | | | | | | | | 1 | 5 | 8 |
| 7 | $[(Et_2N)(ClCH_2CH_2O)P(O)]_2O$ | 170-2/0.03 | 1.4640 | 1.2270 | 68 | 15.0 | 15.0 | 0.1 | 7 | |
| | | | | | | | | 0.5 | 7 | |
| | | | | | | | | 1 | 7 | 1 |

The synthesis of compounds of this type is of interest not only from the viewpoint of preparation of new physiologically active substances but also for the possibility of following the influence of chlorine atoms in these compounds on the character of toxicity in respect to invertebrates and warm-blooded animals. The effect of halogen atoms in organophosphorus compounds on their physiological activity is still insufficiently clear.

In some cases the substitution of alkyl radicals by chloroalkyls is not accompanied by any significant change of insecticidal activity. Forexample, the latter remains the same in diethyl fluorophosphate, ethyl 2-chloroethyl fluorophosphate and di-2-chloroethyl fluorophosphate (5).

In other cases the introduction of halogen produces a slight lowering of the insecticidal activity, as is the case with tetrachlorodiisopropyl fluorophosphate. Its toxicity is some four times less than that of diisoprppyl fluorophosphate (5). Finally, what is specially characteristic of compounds with aromatic radicals, the introduction into an organophosphorus compound of halogen atoms sharply lowers the toxic action on warm-blooded animals (parathion, chlorothion) with but slight lowering of the insecticidal action (8,9).

In view of the fact that the influence of chloro-containing radicals in the esters and ester amides of pyrophosphoric acid had not been studied in the connection with alteration of chemical and physiological properties, it seemed interesting to us to synthesize alkyl 2-chloroethyl esters of pyrophosphoric

their chemical [illegible] insecticidal properties. The [illegible] of pyrophosphoric acid were prepared by Toy's method [illegible] appropriate chlorides of dialkyl phosphoric acid, [illegible] which reaction is shown as follows:

$(ClCH_2CH_2O)_2POCl \rightarrow (ClCH_2CH_2O)_2P(O)OP(O)(OCH_2CH_2Cl)_2$

$(ClCH_2CH_2O)(RO)POCl \rightarrow (ClCH_2CH_2O)(RO)P(O)OP(O)(OCH_2CH_2Cl)(OR)$

$(ClCH_2CH_2O)POCl(NEt_2) \rightarrow (ClCH_2CH_2O)(Et_2N)P(O)OP(O)(NEt_2)(OCH_2CH_2Cl)$

The initial chlorides of bis-2-chloroethyl and alkyl 2-chloroethyl [illegible] were prepared in 52-67% yields. These chlorides were prepared [illegible] of Cook and coworkers (11), and by the reaction of ethylene [illegible] oxychloride with subsequent treatment of the thus formed [illegible] 2-chloroethyl phosphate with diethylamine (12) or alcohol, [illegible] following equations:

$EtO + POCl_3 \rightarrow ClCH_2CH_2OPOCl_2$

$ROH + Et_3N \qquad 2Et_2NH$

$ClCH_2CH_2OP(O)(OR)Cl + Et_3N.HCl \qquad ClCH_2CH_2OP(O)(NEt_2)Cl + Et_2NH.HCl$

[illegible] of various 2-chloroethyl esters of pyrophosphoric acid [illegible] ation at -5°. The purification of crude products was done [illegible] and then by ordinary distillation in vacuum (table 3.). [illegible] products were obtained in 80-90% yields. All alkyl 2-chloroethyl [illegible] phosphoric acid were colorless viscous liquids which [illegible] insecticidal properties which decline with the increased [illegible] atom in the molecule of the ester. It was noted that in esters [illegible] symmetrically located radicals the toxicity is less than in esters [illegible] unsymmetrically located radicals.

## Conclusions.

Several esters of alpha-dialkylphosphono-beta-trichloroethyl phosphoric and 2-chloroethyl phosphoric acids were synthesized.

Previously prepared substances have insecticidal properties.

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